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EXAMINER	
LAM, ANN Y	
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1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/558,936	GOMEZ-ELVIRA RODRIGUEZ ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,8-24,27,28 and 30-43* is/are pending in the application.

4a) Of the above claim(s) *33-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,8,13,19,21-24,27,28 and 30-32* is/are rejected.

7)☒ Claim(s) *2,9-12,14-18 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in the reply filed on April 13, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Objections

Claim 16 is objected to because of the following informalities: "value" should be –valve--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 8, 13, 19, 21,28, 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5, line 5, recites "the sample processing module piston". There is insufficient antecedent basis for this limitation in the claim.

Claim 8, line 2, recites "the rotating drum". There is insufficient antecedent basis for this limitation in the claim.

Claim 13, line 3, recites "the piston". There is insufficient antecedent basis for this limitation in the claim.

Claim 19, line 1, recites "the longitudinally moving rack". There is insufficient antecedent basis for this limitation in the claim.

Claim 21, line 3, recites "the main chamber". There is insufficient antecedent basis for this limitation in the claim.

Claim 31, line 3, recites "the sample distribution module rotating drum". There is insufficient antecedent basis for this limitation in the claim.

Claim 31, line 4, recites "the sample acquisition module hopper or funnel". There is insufficient antecedent basis for this limitation in the claim.

Claim 21 is also vague because it recites the reaction

Claim 28 (and therefore dependent claim 30) is vague because it is not clear if the "suitable radiation detection system" of line 3 is the same as the "reaction detector" of line 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 19 and 21-24 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. 6,994,827 (hereinafter "Safir").

Safir discloses an apparatus and software or firmware that will enable simultaneous reactions in a parallel reactor system having multiple feeds. The parallel reactor comprises two or more reaction vessels for containing liquid reaction mixtures. The two ore more reaction vessels are preferably integral with (e.g., formed or otherwise contained in) a common reactor block, or the vessels can be configured independently of each other. Two or more shaft-driven stirrers (e.g., shaft-driven impellers) can be provided for stirring the reaction mixtures. The shaft-driven stirrers are arranged to correspond to the arrangement of the two or more reaction vessels. The reactor vessel further comprises at least two or more feed lines in fluid communication with each of the two or more reaction vessels. Each of the feed lines provide selective fluid communication between the reaction vessel and one or more reagent sources. Column 2, line 52 to column 3, line 25.

Safir et al. further disclose that the device can include one or more modular feed-line subassemblies (e.g. ferrules), with each of the feed-line subassemblies being adapted to releasably engage a reaction vessel or a reactor block having a reaction cavity that defines or contains the reaction vessel. The feed-line subassembly supports at least two feed lines (and preferably at least three or at least four feed lines)

passing into the reaction vessel through a feed-line subassembly receiving port that is formed in the reaction vessel or the reactor block. Column 3, lines 59-67.

Use of the device is implemented with user-directed reactor-control software or firmware incorporated with the reactor. The feed control effected, preferably with such software or firmware, is preferably applied in connection with methods in which a parallel reactor is provided and comprises four or more semi-continuous or continuous reaction vessels, four or more liquid reagent source vessels, and at least four liquid feed lines providing selectable fluid communication between the four or more liquid reagent source vessels and the four or more reaction vessels.

Safir discloses reactors in which reagents from a reagent source vessels 100 can be fed, through feed lines 300, to the reaction vessels during the course of the reaction. The duration of feed can vary, and can be continuous over a period of time (i.e., temporally continuous) or intermittent over a period of time (i.e., temporally intermittent). In the continuous flow embodiment, a portion of the reaction mixture can be discharged from the reaction vessel during the course of the reaction. The duration of the discharge can be temporally continuous, or temporally intermittent, and in some applications, can be temporally synchronized with the feeding of reagents (e.g. for operation as a continuous reactor, such as a continuous stirred tank reactor). Column 8, lines 34-47.

There can be a number of reaction vessels and/or reagent source vessels (with associated dedicated feed channels). There can be two or more reaction vessels, and

two or more feed channels associated with each of the reaction vessels. Column 8, lines 48-67.

It is also disclose that a feed distribution line could also be used as a discharge line (e.g., by reversing the direction of the pump). In one embodiment, for example, one or more of the 8 liquid feed systems can be run in "reverse" to sample aliquots of the reaction mixture from each vessel, for reaction monitoring or off-line analysis. In this case it may be especially desirable to have additional valves connected to the distribution manifold to allow for sample collection, flushing or washing of the syringe, lines, or valves, or expelling excess reagent to a waste-collection vessel. It may also be desirable to connect one or more input lines supplying each syringe to either a distribution valve to select multiple reagent feeds to one distribution channel, or to an XYZ robotic probe that can select multiple sources. Similarly, the output lines from one or more of the valves may be connected to a distribution valve or to an XYZ robotic probe to enable delivery of aliquots sampled from the reactor vessels to different sample containers. Column 13, line 53 to column 14, line 2.

It is also disclosed that the geometry of the reaction vessel or the reaction cavity or chamber is not, by itself, particularly critical. The reaction vessels can be open or closed, but if open, are preferably contained within a closed reaction chamber or reaction cavity that can be pressurized. Each of the reaction vessels can have a substantially uniform (e.g., circular or oval) cross section (as taken radially). In some embodiments, however, the reaction vessel can have a varying, non-uniform cross section, combining for example both an oval cross section (as taken radially) in a first

(e.g., upper) portion of the reaction vessel and a circular cross section (as taken radially) in a second (e.g., lower) portion. With reference to FIG. 5A, for example, having an oval cross section (or equivalent thereof) in an upper portion 511 of the reaction cavity 510/reaction vessel 500 can advantageously allow for additional space on at least one side, and preferably on both sides of a shaft-driven stirring mechanism, through which multiple feed lines can be provided. In particular, in a preferred or particularly preferred embodiment, each of the two or more, preferably four or more, reaction vessels are defined by or contained in a lower portion of a reaction cavity having a first size and/or shape (e.g., circular shape). The upper portion of the reaction cavity can have a second size (e.g, with a larger cross section) and/or shape (e.g. oval shape) taken radially, relative to the size and/or shape of the lower section, such that there is additional space for passing the feed lines through the upper section to the lower section of the reaction cavity. Column 16, lines 1-30. According to one such staggered control strategy, reactor feed control is effected for each reaction vessel on a rotating serial basis--considering and providing the feed requirements for the first reaction vessel, then the second reaction vessel, then the third reaction vessel, etc., and continuing serially until each of the reaction vessels have been controlled during this first round of control. Control attention is then rotated back to the first vessel, to further consider and provide the feed requirements thereto, and then sequentially through the second reaction vessel, etc. until each of the reaction vessels have been controlled during the second round of control. The sequential control strategy is then repeated until each of the reactions have been completed. Such

sequential control strategy can be effected from a "per reactor" (i.e., "per reaction-vessel") framework--with a single overall control system focusing control attention on all of the feed requirements for a particular reaction at that time, and controlling all of the feed streams to meet those requirements at that time. Alternatively, control can be effected from a "per reagent" (or "per feed line") framework, with multiple independent control systems. Here, each feed line is independently controlled on a staggered basis--that is, independent of the control of other feed lines, with delays or passes (no control effected), as appropriate, to allow for required sequence order of different reagents. Regardless of the control framework, each control event associated with a particular reactor can include, for example, determining the feed requirements for that stage of the reaction--typically by reference to a pre-programed recipe of feed versus time of reaction, but optionally including some real-time or near-real-time feedback loop, with the feed being adjusted to meet a predetermined setpoint (e.g., feeding for pH control, or temperature control). Various feeds can then be added to the reaction vessel to satisfy the then-current feed requirements, for example, by operating the pumps (e.g., syringe pumps), by opening valves in a particular feed line at an appropriate time to select the appropriate receiving vessel and align it to the proper feed in the proper order, by injecting the required fraction of the total amount of that reagent to be added, and then by closing that valve and opening the next one. Rapidly cycling through the valves in each line--under either framework--allows for pseudo-continuous addition of reagents. Column 25, lines 19-38.

The discharge distribution system can provide fluid communication between the reaction vessel and a waste reservoir, a sampling system (e.g., for characterization of a sample taken from the reaction mixture, and/or another reaction system (e.g. for feed to a second reaction vessel in a series). As shown in FIGS. 2A through 2D, for example, the discharge distribution system can comprise a discharge valve 700 or sampling valve (also 700) that provides selective fluid communication between the discharge line 600 and one of a waste collection system, a sample analysis system, a second reaction system, and/or another system. Although shown in FIGS. 2A through 2D with only a single discharge line 600, each reaction vessel 500 could alternatively have two or more discharge lines (for sampling and/or waste). Column 13, lines 36-52.

Additionally, regardless of the particular design, the feed-line subassemblies (e.g. ferrules) can further comprise one or more apertures adapted to support, and preferably sealing support one or more instrumentation lines, including for example, lines for thermocouples, pressure-sensors, pH sensors, in-situ analysis (e.g., fiber-optic probes), etc. Column 21, lines 20-26.

As to claim 1, the Safir stirrer is equivalent to the claimed homogenizer module. The feeding lines to feed samples into the reaction vessels are equivalent to the claimed sample processing module including a series of independent containers, each one of which is intended for receiving one of the samples to be analyzed. [The feeding lines are each inherently a container.] The Safir reaction vessels are equivalent to the claimed reaction chambers, which are provided as many as there are sample processing containers. The Safir reagent source vessels are equivalent to the claimed

reagent and solution management module storing and dispensing the reagents and solution. The instrumentation lines for in-situ analysis (e.g., fiber-optic probes) is equivalent to the claimed data reading module through which the reactions occurring in the reaction chambers are detected and the detected signals are processed. The overall control system (column 25, lines 19-38), or microprocessors or software, is equivalent to the claimed overall controller supervising the process of each of the modules

As to claim 19, the homogenization means consist of a device (the Safir shaft-driven stirrers, e.g., shaft-driven impellers) with mechanical action capable of acting on the samples.

As to claim 21, the feed lines are the inlets connected through a valve to the reaction chamber, to connect to a washing solution, and one or more of the feed lines can also be used to connect to a waste chamber. Column 13, line 53 to column 14, line 2.

As to claims 22-24, Safir discloses a distribution system that provides reagent distribution from each of the reagent source vessels to each of the reaction vessels through dedicated distribution pumps, dedicated feed distribution valves. Column 11, lines 53-67. The pumps may be syringe pumps. Column 12, lines 1-31. A dedicated feed line from a reagent source is equivalent to the claimed cannula. As to claim 24, the pumps and valves, when closed, allows for recirculating of the sample, during the stirring.

Claims 1, 24 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. 6,905,816 (hereinafter "Jacobs").

Jacobs teaches that the disclosed devices/systems include many useful and advantageous features. In some embodiments, the new systems/devices combine sample collection modules with diagnostic devices into a unique combined module, which circumvents the need to transfer biological samples from collection tubes etc. to the diagnostic devices. Alternatively, the systems/devices include sample collection modules that are separate from diagnostic device modules and that can easily be connected at any stage, without having to take the sample out of the collection module. Column 12, lines 10-25.

The disclosed multiplexed diagnostic systems enable a number of disparate tests to be performed simultaneously and under the same conditions, with low cross-reactivity and with high sensitivity and specificity. Column 12, lines 26-32.

Also, the disclosed devices/systems also can be used with an "array of arrays" format, which provides a single device that can be used to process a large number of (same or different) samples in parallel, thus providing a high-throughput environment. For example, by introducing multiple sets of microarrays on a single biochip, one can screen multiple patient samples with clinically clustered tests in one step. Column 12, lines 41-47.

The microfluidics-based devices can also be incorporated into the biochip devices or be used separately. Such microfluidic devices can have chambers or channels that each contain an array of probes that bind complementary analyte targets. This type of an array serves to concentrate related analytes onto a single spot. Bound analytes could be released, using labile linkers on probes, and directed into a second channel or chamber. There the analytes could be further analyzed either on a second array of probes or in a capillary electrophoretic channel. Thus, each analyte is analyzed in two orthogonal dimensions providing a more accurate result. The microfluidic devices can be made on glass, polymers, plastic, silicon, metals, and a variety of other solid substrates. Column 25, line 65 to column 26, line 19.

In one example, there is disclosed a device inside a device type of a system, which utilizes the fast assay time of a microfluidic device for analytical assays. There are a number of different ways that this type of device can be implemented. For example (FIGS. 22A and 22B and 23A and 23B), in one device (FIG. 22A), a central chamber has a set of probes, which are placed at the intersection of an orthogonal artery feeding into another chamber. The probes attached at this nodal point are non-specific in that they bind to a set of target molecules that are unique and yet have at least one similar characteristic. In a way, these nodes act at points in the stream where similar analytes are concentrated. Once this part of the assay is complete, the orthogonal artery is activated and transports each concentrated target set into separate chambers where they are further analyzed into unique positions, based on a second set of interactions. Thus, this system incorporates two orthogonal detection probes and will

thus have a much better detection capability. Another advantage of this type of system, besides being a fast and improved detector, is that it can be combined with other types of biochip devices for enhancing their performance. Column 26, lines 32-52.

Moreover, Jacobs further discloses that the devices can be processed and analyzed using automated processing, such as robotic and computer-controlled screening, scanning, and delivery of results. The new devices, such as diagnostic biochips, can be processed using multiple dyes/colors. Assays can be performed either simultaneously or sequentially. Assays can use either single unique probes for each analyte or multiple unique probes for each analyte. Column 12, lines 48-58.

It is also disclosed that various mixing mechanisms can be utilized, and that mixing during incubation helps decrease the binding time (column 20, lines26-41.)

As to claim 1, the mixing mechanism is equivalent to the claimed homogenizer module. The sample collection modules for combination with the diagnostic modules for parallel assays are collectively equivalent to the claimed sample processing module with a series of independent containers. The diagnostic modules are collectively equivalent to the claimed reaction module with reaction chambers. Figures 22A and 22B disclose a microfluidic device, and the skilled artisan would have recognized that the circular elements are reagent sources (see also column 26, lines 32-52.) A sensor or detector is understood to be included (see column 12, lines 48-58 and column 26, lines 32-52.) Optoelectronic detecting means is also disclosed in column 18, lines 23-34.

As to claim 24, the mixing mechanism is equivalent to a system of stirring or moving the liquid sample. A pumping system (vacuum suction device or pipetman, or electrophoresis (column 25, lines 34-42.) The pumping system is capable of recirculating the sample.

As to claim 27, Jacobs discloses immobilization on a microarray, as discussed above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. 6,905,816 (hereinafter "Jacobs"), in view of U.S. 7,118,907 (hereinafter "Williams").

.While Jacobs disclose use of optoelectronic detection means in general (column 18, lines 23-34), Jacobs is silent as to a CCD camera, optical filter and use of evanescent detection mode. However it is understood from the Jacobs disclosure that the device is not limited to a particular detection technique.

Moreover, Williams teaches a microfluidic device for analyzing a reaction, wherein the device includes immobilization zones within a microchannel (column 5, lines 30-48).An evanescent light field is set up by total internal refection (TIR) of a laser beam at the glass-aqueous solution interface. In certain aspects, the TIR illumination field is continuously imaged at video-rate with an intensified charge couple device (ICCD) camera. Column 25, lines 4-31.

Suitable illumination sources, such as pulsed or continuous wave conventional gas and solid-states lasers, tunable dye lasers, the like may be used. Additionally, various filters, diffraction gratings, mirrors, lenses and other optical elements may be used to manipulate and interact with the illuminating and emitted radiation as desired. Column 34, lines 30-50. See also column 46, lines 48-59. for optical filters.

It would have been obvious to the skilled artisan to utilize the detection elements disclosed by Williams as the specific type of optical detecting elements in the Jacobs device since Jacobs does not limit the detector to any particular type, and thus the skilled artisan would look to the art for types of detectors that can be used, such as that disclosed by Williams.

Allowable Subject Matter

Claims 2, 9-12, 14-18 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 5, 8, 13, 31 and 32 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

U.S. 20030087443 (Pressman) discloses an apparatus to extract samples and for slide based testing. Disclosed are mixer to homogenize the specimen, handling mechanism, and receptacles that are moved and a mechanically actuated cannula.

U.S. 4,859,610 (Maggio) discloses a vessel with an insert that defines an incubation chamber and includes a screen to allow fluid to pass but exclude passage of unextracted sample components from entry into the incubation chamber. The device homogenizes by rotating an insert.

U.S. 6,706,519 (Kellog) discloses a disc with multiple microfluidic structures to process samples simultaneously.

.Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Thurs. 9-7:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641